REMARKS

The Office Action of July 17, 2003 presents the examination of claims 1-17 and 32. Claims 18-29 and 33 stand withdrawn from consideration. The present paper cancels claims 1-33, and presents new claims 34-50, directed to the subject matter of elected Group I, an expression cassette, vectors comprising that cassette, cells transformed with the cassette and a method for transforming pluripotent cells using the cassette.

Applicant reserves the right to file an application directed to the non-elected subject matter pursuant to 35 USC § 120.

Support for the new claims

Written description of the embodiments of newly presented claim recitations is found in the specification as follows.

A "polynucleotide comprising a cardiac muscle-specific promoter" is described at, e.g. page 9, line 5. Operative linkage to "a polynucleotide comprising a polynucleotide encoding extracellular and transmembrane domains of a receptor expressed by B or a T cell" is described at, e.g. page 8, last paragraph.

A "polynucleotide comprising an enhancer" is described at, e.g. page 10, line 5. That such enhancer is "operative in a

mammalian ES cell, primordial cell or bone marrow stromal cell" is described at, e.g. page 13, line 21.

A "promoter constitutively operative in a mammalian ES cell, primordial cell or bone marrow stromal cell" is described by the example of the PGK promoter and as much is admitted by the Examiner in citing the Gainer et al. reference. Operative linkage of such promoter to "a secreted immunosuppressive protein" is described at, e.g. page 11, second to last paragraph from the end of the page.

The list of B or T cell receptors to be expressed as recited in claims 39, etc. is found at the last paragraph on page 8.

The electrophysiologic and muscarinic receptor properties recited in claims 47-49 are described at page 16 in the third paragraph.

Claim objections

Applicant has presented new claims numbered from 34 in accord with the renumbering of the claims by the Examiner. The new claims each begin with an article. The term "non-immunogenic receptor" is no longer employed in the claims.

The "recitations a) and c)" are no longer present in the claims. However, Applicant would point out that these recitations, while broad, are not "meaningless". As the

Examiner notes, "any receptor on the surface of a non-stem cell would meet this limitation." The Examiner is reminded that one aspect of the invention is the isolation of stem cells that are expressing the nucleic acids encoded by the cassette. Any cell surface marker not normally present on the surface of the stem cell, but present because it is encoded by the claimed cassette, is indeed useful for this purpose.

Objection to the specification

A section entitled "Brief Description of the Drawings" has been added to the specification as required. Support for the description of the figures added is provided at page 21, line 5 and page 22, line 8.

Rejection under 35 USC § 101

Claim 32 is rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Claim 32 has been canceled, rendering the rejection moot.

However, Applicant submits that the Examiner position on this issue is incorrect. Claim 32 recited a method of transforming stem cells, human or otherwise. Such subject matter is within the statute. The Examiner is further reminded that cells and cell lines, including human cells and even human embyronic stem cells, transformed or otherwise, are statutory

subject matter. It is human beings as whole organisms that are not patentable subject matter.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-3 and 9-11 are rejected under 35 U.S.C. § 112, second paragraph, for recitation of various terms and phrases. Claims 1-3 and 9-11 have been canceled, rendering these grounds of rejection moot. Applicant submits that the terms raising the grounds of rejection are not used in the newly presented claims and so this rejection should not be applied to them.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 32 is rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement by the specification. Claim 32 has been canceled, rendering this rejection moot.

New claim 49 recites that the cells are transformed *in vitro*, which method has been explicitly admitted by the Examiner to be enabled. Thus, the instant rejection should not be applied to the pending claims.

Applicant in no way acquiesces to the Examiner's position that *in vivo* transformation methods using the present invention are not enabled.

Anticipation rejections

Claims 1-5, 12 and 16 were rejected under 35 U.S.C. § 102(b) as anticipated by Segre et al. Claims 1-5, 12 and 16 are canceled, rendering this rejection moot. Applicant submits that the reference is not applicable against the new claims.

Segre et al. describe a cloned nucleic acid encoding a parathyroid hormone. This is not encompassed by the present claims and therefore these claims should be found free of this rejection.

Notwithstanding that, the Examiner should note that the Segre reference is also silent as to the limitation in the prior claim 2 that the expressed gene is one "not expressed naturally on the pluripotent progenitor cells". Nor would such a property be expected to be inherent. Being a hormone, the protein product of the parathyroid hormone-encoding nucleic acid would be expected to be secreted from the cell into the surrounding medium and not "on the pluripotent progenitor cells".

Claims 1, 2, 4, 5, 12 and 16 were rejected under 35 U.S.C. § 102(b) as being anticipated by Reppert et al. Claims 1, 2, 4, 5, 12 and 16 are canceled, rendering this rejection moot. Applicant submits that the reference is not applicable against the new claims.

Reppert et al. describe a cloned nucleic acid encoding a melatonin receptor. This is not encompassed by the present

claims and therefore these claims should be found free of this rejection.

Notwithstanding the above, the Examiner should note that the Reppert reference is also silent as to the limitation in the prior claim 2 that the expressed gene is one "not expressed naturally on the pluripotent progenitor cells", and the Examiner has not provided any substantial evidence or scientific reasoning to believe such property is inherent to a melatonin receptor gene.

Claims 1, 2, 4, 5 and 16 were rejected under 35 U.S.C. § 102(b) as being anticipated by Harlan et al. Claims 1, 2, 4, 5, 12 and 16 are canceled, rendering this rejection moot. Applicant submits that the reference is not applicable against the new claims.

Harlan et al. describe a cloned nucleic acid encoding a cell surface antigen B7 linked to a rat insulin promoter. This is not encompassed by the present claims and therefore these claims should be found free of this rejection.

Rejection under 35 U.S.C. § 103(a)

Claims 1-6, 10, 12, 13, 15-17 and 32 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Klug et al. (J. Clin. Invest. 1996), and Gaines et al. (Biotechniques 1999) in further view of Griscelli et al. (Hum. Gene Ther. 1998) and Wolfgang-M.

et al. (J. Mol. Cardiol. 1997). Claims 1-6, 10, 12, 13, 15-17 and 32 have been canceled, rendering this rejection moot. Applicant submits that this rejection is not applicable to the present claims.

The cited references fail to establish *prima facie* obviousness of the presently claimed invention. In particular, the cited references do not describe or suggest each and every limitation of the present claims. For example, at least the recitation of "at least one IRES operatively linked to at least one polynucleotide encoding an angiogenesis factor" is not described or suggested by any reference, and is therefore absent from their combination.

Second, the instant invention provides a result that is not expected by the skilled artisan who reads the cited references. For instance, cells having the properties of ventricular cardiac cells are obtained by utilizing the expression cassette of the instant invention, transforming ES cells and selecting for the expression of the extracellular and transmembrane domains of a receptor expressed by B or a T cell encoded by the cassette. This is shown, e.g. by the results of the experiment described in Example 1 of the present specification. Figure 2 shows data obtained from electrophysiologic measurements of cells produced in Example 1. See, pp. 21-25 of the specification. Such a

result would not be expected by the skilled artisan reading the cited references.

For example, comparison against the G418-selected population of cells obtained by Klug et al. shows expression of both atrium-specific MLC-2a and ventricle-specific MLC-2v in about equal proportion. See, Fig. 3 of the reference at page 220. Comparison to fluorescence-activated cell sorting as performed by Griscelli et al. provides only about 67% purification. See, the last line of col. 2 at page 687. Thus, a mixed population of cells would be expected to be obtained by the selection methods employed using the cassettes described by the prior art cited.

For all of the above reasons, Applicant submits that the invention as presently claimed is unobvious in view of Klug et al. (J. Clin. Invest. 1996), and Gaines et al. (Biotechniques 1999) in further view of Griscelli et al. (Hum. Gene Ther. 1998) and Wolfgang-M. et al. (J. Mol. Cardiol. 1997).

The present application well-describes and claims patentable subject matter. The favorable action of allowance of the pending claims and passage of the application to issue is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell (Reg. No.

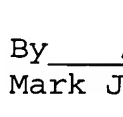
36,623) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), Applicants respectfully petition for a three (3) month extension of time for filing a response in connection with the present application. The required fee of $475.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By 
Mark J. Nuell, #36,623

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

DRN/mua
0690-0115P